REMARKS

In the Office Action dated July 17, 2003 the Examiner rejected the specification as containing nucleotide sequences that did not have a paper copy and a computer readable copy of the sequence listing. Applicant has provided such and believes that these sequences are now in order.

Claim 11 was objected to because the claim was written to encompass multiple inventions. Claim 11 has been amended to more specifically define its scope by incorporating Claim 14.

Claims 1, 3, 12-13, 19 and 22 were rejected under 35 USC 112, first paragraph, as containing subject matter which is not described in the specification. Claims 1, 11, 12 and 19 were rejected under 35 USC 102(b) as being anticipated by a series of scientific articles. Applicant respectfully believes it to be somewhat confusing that the same claims are rejected on the grounds that they have not been reduced to practice yet and at the same time have been reduced to practice by others. However, as explained below, Applicant believes neither to be the case. The claims have been amended to more clearly reflect the intent of the invention.

The Examiner rejected claims 1, 3, 11-13, 19 and 22 as not being described in the specification. Applicant has amended the claims so that they are now drawn to "ferritin-H or conservatively modified variance thereof" instead of simply "derivatives thereof". It is Applicant's understanding that such terminology has been deemed acceptable as explained in the M.P.E.P. Section 2422.03, seventh paragraph. Applicant believes that the M.P.E.P. allows such a description because, although the effects of replacing amino acid in a peptide can never be absolutely known, those skilled in the art will appreciate that most single amino acid exchanges results in a peptide that is at least partially functional. In addition, exchanging similar peptides, such as leucine and isoleucine rarely have a major impact on the structure and function of an enzyme, because their side chains are so similar. Those skilled in the art will appreciate that there are a variety of amino acids

very similar to one another and exchanging them results in a conservative variance of the original peptide.

Because erythroid precursor cells are generally capable of taking up free ferritin-H, the language in the claims drawn toward the use ligands has been removed. Erythroid precursor, globin-producing cells have receptors that allow them to uptake ferritin-H. Ferritin-H is a relatively small polypeptide of only about 21 kDa. It is, therefore, small enough to enter into the nuclear membrane.

The claims have also all been drawn to treatment of sickle cell disease. Because the specification teaches a method of depressing beta globin production by expressing ferritin-H, Applicant believes the specification supports claims drawn to increasing intracellular ferritin-H concentrations, thereby suppressing expression of beta globin genes. Furthermore, prior art discloses a variety of methods of transforming cells to incorporate foreign genes. U.S. Patent No. 6,140,111 to Ridiere et al. describes transvection in significant detail. Also, column 2, lines 45-52 cite several other prior art patents that discuss the use of retroviral vectors that insert genes into the genomes of mammalian cells. Applicant therefore believes that these techniques are well known in the art and that the details of their use are not necessary to support the specification.

The Examiner also has pointed out that molecular interactions that take place *ex vivo* do not necessarily translate into *in vivo* results, and that since the filing of the application, no positive clinical results have been achieved. Applicant acknowledges that *ex vivo* and *in vivo* conditions are always different. However, suppression of beta globin genes by ferritin-H have been shown to take place intracellularly. The major distinction between the cells used *ex vivo* in Applicant's experiments and *in vivo* intracellular chemistry lie in the reproductive pathways. Although these genetic differences often cause significant problems in cancer research, they do not pose the same uncertainties when studying iron management. In addition, the FDA has very strict guidelines for

developing clinical treatments and it often takes many years to produce positive results. That ferritin-H therapy is neither routine nor accepted as a treatment for sickle cell disease is in fact strong evidence of the novelty of the present invention.

The Examiner also cited the article to Adams et al. as anticipating the present invention. Generally, the Adams et al article describes giving patients with sickle cell anemia transfusions in order to prevent the first stroke. Applicant believes that this article does not disclose the present invention. Because blood donations are only taken from adults, any blood transfusions as described in this article would be comprised of adult blood. Adult blood does not contain ferritin-H so that any ferritin in a blood transfusion would be ferritin-L or another ferritin protein. Only embryonic erythroid cells contain significant amounts of ferritin-H. Therefore, nothing in this article would suggest that a protein that is not present in such a blood transfusion would have any effect on sickle cell disease. The only suggestions made by the Adams et al article is that the addition of normal adult hemoglobin can reduce blood-flow velocity as detected by ultrasonography.

For all the above reasons, Applicant now believes that the application should be in condition for allowance and such action is earnestly solicited. If, for some reason, any other issues remain, a telephone conference with the Examiner is respectfully requested.

Respectfully submitted,

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